UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

IN RE BIOPURE CORPORATION SECURITIES LITIGATION	**)**	**Master Docket No. 1:03-CV-12628 (NG)**
	)	**Assigned to Judge Nancy Gertner**

DEFENDANTS' RESPONSE TO PLAINTIFFS' POST-ARGUMENT SUPPLEMENTAL SUBMISSION IN SUPPORT OF PLAINTIFFS' MOTION TO AMEND COMPLAINT

The Plaintiffs have submitted what they appear to deem a "smoking gun" in support of their motion for leave to add the SEC's allegations into their complaint. The Plaintiffs' "smoking gun" -- *i.e.* that the July 30, 2003 letter about trauma contained (in part) identical questions that were in the BLA Letter of the same date -- was apparently only learned by the Plaintiffs by reading the "Defendants' disclosure" in pleadings filed in the SEC action. Pl. Mem. at 2 ("Plaintiffs have now learned . . ."). In substance, this "additional fact, previously unknown" by the Plaintiffs (Pl. Mem. at 2) had been publicly disclosed by Biopure since 2003 in the very press release that triggered the filing of the Plaintiffs' complaint:

> The questions in the FDA's trauma letter were the same as some of the questions in the BLA complete response letter and had two additional questions . . . .

Biopure Corp., December 24, 2003 Press Release. Indeed, this very sentence is quoted in the Plaintiffs' proposed amended complaint at paragraph 162.

Just as the purported "revelation" of this two-year old, stale piece of information raises nothing new, neither does the Plaintiffs arguments based upon it. The Company has admitted since its first disclosure on the topic that the orthopedic surgery BLA and the trauma IND involved the same underlying data. See Biopure's December 24, 2003 Press release. All that is demonstrated by Biopure's pleading in the SEC action (as well as its December 2003 press release) is the uneventful occurrence of FDA questions about common data -- but not a link in

any material sense between the two separate regulatory tracks for the in-hospital trauma protocol and the orthopedic surgery BLA.

In a nutshell, the Plaintiffs argue that, because the questions in the two letters were the same, communications about the trauma hold must have amounted to communications about the BLA as well; "safety concerns" expressed about trauma must also be "safety concerns" about the BLA; and accordingly, the clinical hold must have been material to the BLA. The Plaintiffs have only demonstrated their dearth of knowledge concerning FDA's own regulations which, as a matter of law, dictate that the trauma hold for an in-hospital indication and the July 30 letter regarding the hold were not communications about the BLA. The FDA's clinical hold regulation, 21 C.F.R. § 312.42, provides: "A clinical hold is an order issued by FDA to the sponsor to delay a proposed *clinical investigation* or to suspend an ongoing investigation. *The clinical hold order may apply to one or more of the investigations covered by an IND. . . . It will identify the studies under the IND to which the hold applies*." (Emphasis added). In other words, a clinical hold (and the communications about it) apply only to an investigation -- *i.e.* the trauma trial -- covered by a given IND. While the FDA "may" expand a hold beyond a single investigation covered by the IND before it, the BLA was neither an investigation, or "study," nor was it "under the IND to which the [trauma] hold applie[d]." There simply is no regulatory basis for the FDA to communicate about a BLA through its concerns raised in a clinical hold on an investigation -- clinical holds apply to "investigations," not BLA's. The mere fact that identical questions were raised *about data* underlying separate indications does not change that circumstance.

To shore up that hole in the Plaintiffs' asserted, but unalleged (at least beyond conclusory allegations) theory, the Plaintiffs contend that the identity of questions in the trauma letters and

BLA letter must supply the missing link. It does not. As explained in detail in previous memoranda, a BLA is a culmination of clinical investigations and data gathering about a biologic within a particular indication – *i.e.*, a specific patient class in a specific setting. Here, Biopure submitted its BLA based on near twenty previous investigations and the proposed indication in the BLA was orthopedic surgery. The trauma trial IND, by contrast, was an investigation concerning an in-hospital trauma indication. While the BLA and the trauma protocol involved distinct indications requiring distinct risk/benefit analyses (*i.e.* "safety" as previously briefed at length), both involved Hemopure. And as the Company has disclosed, the trauma protocol, while distinct in indication, was nonetheless (and logically) submitted in reliance on some of the same data that supported the BLA -- the data submitted in the IND came from the same pool of information that Biopure spent years compiling for the BLA. This does not change the fact that the FDA's review of the IND submission was limited to how the product would be administered in a specific proposed trial involving trauma patients at a much higher dosage than previously administered -- separate from the BLA.

The Plaintiffs' assertions that the identity of questions in the two letters "vitiates" and "belies" the Defendants' arguments on the motion to amend is wishful thinking. The Plaintiffs criticize Biopure's argument that "when [the FDA] did communicate about the BLA . . . they did not raise those questions about trauma [from April]. . . . we have the July 30 BLA Letter, and its not about trauma or those questions." Pl's Mem. at 3 (quoting Mr. Buhlman). That statement is unequivocally correct. One need only read the BLA Letter to determine that there is nothing in it that references safety concerns in the trauma clinical hold. Biopure *did not* argue in the SEC action (as Plaintiffs seem to imply) that the identical questions were specific to safety and the clinical hold -- because they were not. The questions were, as can be gleaned from the July 30

BLA Letter, questions about data -- data that was common to both the BLA and the trauma protocol.

Similarly, the Plaintiffs attack Biopure's argument that "there is no factual basis to ask this Court to infer that the trauma clinical hold delayed or slowed down the BLA review" and that there is "no factual basis to draw that link." *Id.* at 4 (quoting Mr. Buhlman). That the FDA asked the same data questions in the two letters changes nothing here. There was not a single particularized fact alleged previously, nor one argued now, that shows that the trauma hold impacted the timing of the BLA review. That the FDA asked identical data questions shows just that -- it asked about data -- not that the trauma hold slowed down the BLA.

Finally, the Plaintiffs view as "belied" the argument that "none of what [plaintiffs have] pleaded amounted to knowledge by anyone at Biopure that the trauma hold and BLA were in any way interrelated." Id. Again, the Company has acknowledged since its first disclosure on the topic that the trauma protocol and the BLA relied upon common data -- but that fact does not somehow amount to knowledge by Biopure that communications about the clinical hold (limited by regulation to concern the clinical hold only) should be deemed to communications about the BLA. It does not change the fact that the proposed trauma protocol and orthopedic surgery BLA were separate indications, that the FDA treated them separately (as it must under its own regulations), and that there is no fact alleged showing that the FDA ever communicated otherwise.

Conclusion

For the forgoing reasons, and those stated in Defendants' opposition to Plaintiffs' motion for leave to amend should be denied.

March 24, 2006

Respectfully submitted,

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By their attorneys,

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CERTIFICATE OF SERVICE

I hereby certify that a true copy of the above pleading was electronically served upon the attorneys of record for all parties on March 24, 2006.

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